Amendments to the Claims

This listing of claims is intended to replace all prior versions and listings of claims in the above-identified application.

1. (currently amended) A compound comprising a gonadotrophin releasing hormone (GnRH) analogue conjugated to a steroid hormone or a progesterone derivative ~~moiety, or a C11, C17, or C21 hydroxy derivative thereof,~~ which is able to bind to a plasma hormone binding protein, wherein the steroid hormone is estradiol, progesterone, cortisol, corticosterone, estrone, testosterone or dihydroxytestosterone, and wherein the progesterone derivative is 11α-hydroxyprogesterone or 21-hydroxyprogesterone.

2. (original) A compound according to Claim 1 wherein the GnRH analogue is a peptide analogue.

3. (original) A compound according to Claim 2 wherein the GnRH analogue is a nonapeptide or a decapeptide.

4. (previously presented) A compound according to Claim 1 wherein one of the amino acid residues of the GnRH analogue is a D-amino acid.

5. (previously presented) A compound according to Claim 4 wherein the D-amino acid is D-Lys.

6. (previously presented) A compound according to Claim 4 wherein the D-amino acid is at position 6.

7. (previously presented) A compound according to Claim 1 wherein the GnRH analogue is a GnRH antagonist.

8. (original) A compound according to Claim 7 wherein the GnRH antagonist is [AcD-Nal^1, D-Cpa^2, D-Pal^3, Arg^5, D-Lys^6, D-Ala^{10}]GnRH, or [Ac-ΔPro^1, D-Fpa^2, D-Trp^3, D-Lys^6]GnRH.

9. (previously presented) A compound according to Claim 7 wherein the GnRH antagonist is Cetrorelix, Ganirelix, Abarelix, Antide, Teverelix, FE200486, Nal-Glu, A-75998, A-76154, A-84861, D-26344, D-63153, ramorelix, degarelix, NBI-42902, Org-30850, detirelix, iturelix, TAK-013, TAK810, AN 207, AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Leu-Arg-Pro-D-Ala-NH_2; Ac-ΔPro-D-Fpa-D-Trp-Ser-Tyr-D-Lys-Leu-Arg-Pro-Gly-NH_2; AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Lys-Leu-Arg-D-Ala-NH_2; D-Pal-Ser-Arg-D-Lys-Leu-Arg-Pro-D-Ala-NH_2; AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Lys-Arg-Pro-D-Ala-NH_2; [D-Pyr^1, D-Phe^2, D-Trp^{3-6}]GnRH; D-Lys^6Antide; Lys^5 Antide or Lys^8 Antide.

10. (previously presented) A compound according to Claim 1 wherein the GnRH analogue is a GnRH agonist.

11. (previously presented) A compound according to Claim 10 wherein the GnRH agonist is pGlu-His-Trp-Ser-Tyr-D-lys-Leu-Arg-Pro-GlyNH_2, Lupron, Zoladex, Supprelin, Synarel, Buserelin, leuprolide, goserelin, deslorelin, ProMaxx-100, avorelin, histrelin, nafarelin, leuprorelin or triptorelin.

12-14. (cancelled)

15. (currently amended) A compound according to Claim 1 wherein the compound retains the *in vivo* hormonal activity of the steroid hormone ~~moiety~~ or progesterone derivative ~~thereof~~.

16. (currently amended) A compound according to Claim 1 wherein the compound has no *in vivo* hormonal activity of the steroid hormone ~~moiety~~ or progesterone derivative ~~thereof~~.

17. (currently amended) A compound according to Claim 1 wherein the steroid hormone or progesterone derivative ~~moiety~~ binds to a plasma hormone binding protein *in vivo*.

18. (previously presented) A compound according to Claim 1 wherein the hormone binding protein is a globulin.

19. (original) A compound according to Claim 18 wherein the plasma hormone binding protein is cortisol binding globulin (CBG), sex hormone binding globulin (SHBG), or progesterone binding globulin (PBG) or albumin.

20. (currently amended) A compound according to Claim 1 wherein the conjugated GnRH analogue and the steroid hormone ~~moiety~~ or progesterone derivative are cleavable.

21. (currently amended) A compound according to Claim 1 wherein the GnRH analogue and the steroid hormone ~~moiety~~ or progesterone derivative are directly conjugated.

22. (currently amended) A compound according to Claim 1 wherein the GnRH analogue and the steroid hormone ~~moiety~~ or progesterone derivative are conjugated via a linking group.

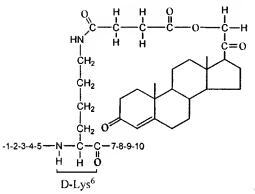
23. (previously presented) A compound according to Claim 22 wherein the linking group comprises a succinate linker or a derivative thereof.

24. (currently amended) A compound according to Claim 1 wherein the GnRH analogue has a D-lysine residue, and the GnRH analogue is conjugated to the steroid hormone or progesterone derivative ~~moiety~~ via the D-lysine.

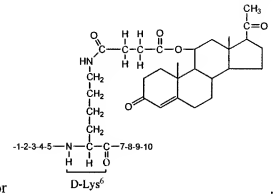
25. (previously presented) A compound according to Claim 1 which has a longer half-life *in vivo* than native GnRH.

26. (previously presented) A compound according to Claim 1 which has a longer duration of activity *in vivo* than native GnRH.

27. (previously presented) A compound according to Claim 1 having the formula



or



.

28. (previously presented) A compound according to Claim 1 which is: AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Leu-Arg-Pro-D-Ala-NH_2 conjugated to 21-hydroxyprogesterone 21-succinate at the ε amine of D-Lys at position 6; Ac-ΔPro-D-Fpa-D-Trp-Ser-Tyr-D-Lys-Leu-Arg-Pro-Gly-NH_2 conjugated to 21-hydroxyprogesterone 21-succinate at the ε amine of D-Lys at position 6; AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Lys-Leu-Arg-D-Ala-NH_2 conjugated to 21-hydroxyprogesterone 21-succinate at the ε amine of Lys at position 7; D-Pal-Ser-Arg-D-Lys-Leu-Arg-Pro-D-Ala-NH_2 conjugated to 21-hydroxyprogesterone 21-succinate at the N-terminal amine of D-Pal; AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Lys-Arg-Pro-D-Ala-NH_2 conjugated to 21-hydroxyprogesterone 21-succinate at the ε amine of Lys at position 7; or [$DLys^6$]GnRH conjugated to l lα-hydroxyprogesterone 11-succinate at the ε amine group of the D-Lys at position 6.

29. (previously presented) A compound according to Claim 1 which is bound to a plasma hormone binding protein.

30. (original) A compound according to Claim 29 wherein the plasma hormone binding protein is CBG, SHBG, or albumin.

31. (previously presented) A pharmaceutical composition comprising a compound according to Claim 1 and a pharmaceutically acceptable excipient, carrier or diluent.

32. (original) A pharmaceutical composition according to Claim 31 which is suitable for oral administration.

33. (original) A pharmaceutical composition according to Claim 31 which is a slow-release formulation.

34. (canceled)

35. (previously presented) A method of reducing the fertility of an individual comprising administering a compound according to Claim 1 to the individual.

36. (canceled)

37. (currently amended) A method of treating ~~combating~~ a hormone-dependent disease or condition comprising administering a compound according to Claim 1 to an individual in need thereof.

38. (canceled)

39. (previously presented) A method according to Claim 37 wherein the hormone-dependent disease or condition is selected from a hormone-dependent cancer, benign prostatic hypertrophy, endometriosis, uterine fibroids, premenstrual syndrome, polycystic ovarian syndrome, hirsutism, acne vulgaris, precocious puberty, acute intermittent porphyria, cryptoorchidism and delayed puberty.

40. (previously presented) A method according to Claim 39 wherein the hormone-dependent cancer is breast cancer, prostate cancer, uterine cancer or endometrial cancer.

41. (currently amended) A method of treating ~~combating~~ infertility comprising administering a compound according to Claim 1 to an individual in need thereof.

42. (canceled)

43. (previously presented) A method of modulating the production of gonadotrophins or sex hormones *in vivo* comprising administering a compound according to Claim 1 to an individual.

44. (canceled)

45. (currently amended) A method of modifying a GnRH analogue so that it has an increased *in vivo* half-life compared to GnRH, the method comprising conjugating the GnRH analogue to a steroid hormone or progesterone derivative ~~moiety, or a C11, C17, or C21 hydroxy derivative thereof,~~ which is able to bind to a plasma hormone binding protein, wherein the steroid hormone is estradiol, progesterone, cortisol, corticosterone, estrone, testosterone or dihydroxytestosterone, and wherein the progesterone derivative is 11α-hydroxyprogesterone or 21-hydroxyprogesterone.

46. (currently amended) A method of modifying a GnRH analogue so that it has an increased duration of activity *in vivo* compared to GnRH, the method comprising conjugating the GnRH analogue to a steroid hormone or progesterone derivative ~~moiety, or a C11, C17, or C21 hydroxy derivative thereof,~~ which is able to bind to a plasma hormone binding protein, wherein the steroid hormone is estradiol, progesterone, cortisol, corticosterone, estrone, testosterone or dihydroxytestosterone, and wherein the progesterone derivative is 11α-hydroxyprogesterone or 21-hydroxyprogesterone.

47. (currently amended) A method according to Claim 45 wherein the conjugating step comprises conjugating the GnRH analogue and the steroid hormone ~~moiety~~ or progesterone derivative ~~thereof~~ via a linking group.

48. (currently amended) A method according to Claim 45 further comprising binding the steroid hormone ~~moiety~~ or progesterone derivative ~~thereof~~ to a plasma hormone binding protein.

49. (original) A method according to Claim 48 wherein the plasma hormone binding protein is CBG, SHBG, or albumin.

50. (previously presented) A method according to Claim 45 further comprising determining the *in vivo* half-life of the conjugated GnRH analogue.

51. (previously presented) A method according to Claim 50 further comprising comparing the *in vivo* half-life of the conjugated GnRH analogue with the *in vivo* half-life of GnRH to identify a GnRH analogue having an increased *in vivo* half-life compared to GnRH.

52. (previously presented) A method according to Claim 35 wherein the compound is present in a pharmaceutical composition that comprises a pharmaceutically acceptable excipient, carrier or diluent.

53. (previously presented) A method according to Claim 37 wherein the compound is present in a pharmaceutical composition that comprises a pharmaceutically acceptable excipient, carrier or diluent.

54. (previously presented) A method according to Claim 41 wherein the compound is present in a pharmaceutical composition that comprises a pharmaceutically acceptable excipient, carrier or diluent.

55. (previously presented) A method according to Claim 43 wherein the compound is present in a pharmaceutical composition that comprises a pharmaceutically acceptable excipient, carrier or diluent.

56. (currently amended) A method according to Claim 46 wherein the conjugating step comprises conjugating the GnRH analogue and the steroid hormone ~~moiety~~ or progesterone derivative ~~thereof~~ via a linking group.

57. (currently amended) A method according to Claim 56 further comprising binding the steroid hormone ~~moiety~~ or progesterone derivative ~~thereof~~ to a plasma hormone binding protein.

58. (previously presented) A method according to Claim 57 wherein the plasma hormone binding protein is CBG, SHBG, or albumin.

59. (previously presented) A method according to Claim 46 further comprising determining the *in vivo* duration of activity of the conjugated GnRH analogue.

60. (previously presented) A method according to Claim 59 further comprising comparing the *in vivo* duration of activity of the conjugated GnRH analogue with the *in vivo* duration of activity of GnRH to identify a GnRH analogue having an increased *in vivo* duration of activity compared to GnRH.